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Estimating the sensitivity of a prostate cancer screening programme for different PSA cut-off levels: a UK case study

Short title: Sensitivity of screening programme for prostate cancer

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Abstract

Introduction: Policy decisions about prostate cancer screening require data on the natural history of histological cancers and the resulting impact of screening. However, the gold standard procedure required to identify true positive histological cancer is a full autopsy of the gland which is not possible in screening studies, leading to verification bias. We aim to estimate the sensitivity of a prostate cancer screening round (PSA result to diagnosis) relative to histological cancer.

Methods: We developed a framework combining data on UK screened and non-screened prostate cancer populations originating from a single round of population-based PSA testing among UK men aged 50-69 years, prostate cancer incidence data, and needle biopsy data from the published literature.

Results: Sensitivity of a screening round was highest at age 65-69 years at 33% (95% CI: 30%-37%) and 24% (95% CI: 21%-28%) for PSA cut-off levels of 3ng/ml and 4ng/ml, respectively. Sensitivity was lowest at age 50-54 at 15% (95%CI: 12%-17%) and 9% (95%CI: 8%-11%) for PSA cut-off levels of 3ng/ml and 4ng/ml, respectively. In contrast, the clinical detection rate in the absence of mass screening, relative to histological cancer, varied between 0.2%-0.7% at age 50-54 and 1.2%-2.7% at age 65-69 from 1995 to 2012.

Conclusions: The framework enabled the sensitivity of a prostate cancer screening round relative to histological cancer diagnosis to be estimated and provides a basis to determine the impact and cost-effectiveness of prostate cancer screening. The approach could be adapted to inform the sensitivity of other biomarkers, cancers and screening programmes.

Keywords: Screening; sensitivity; prostate cancer; evidence synthesis; overdiagnosis; overdetetection

Highlights

- A framework to estimate the sensitivity of prostate cancer screening is proposed
- Sensitivity was highest at age 65-69 years for two PSA cut-off levels
- Clinical detection in the absence of mass screening was relatively small

1. Introduction

Prostate cancer represents the highest incidence of all cancers in men in Europe and the US (23% of all cancers) and is the third main cause of cancer mortality (9% of all cancer deaths).[1] Questions remain about the scale of the contribution of early detection and treatment.[2-5] Many screen-detected cases would never have become clinically apparent within the man's lifetime, as undiagnosed histological cancer increases with age from 2% (95%CI: 1-3%) between 20-29 years-of-age to 69% (95%CI: 51-83%) by 90-99 years-of-age.[6]

Public policy decisions for prostate cancer screening programmes rely on natural history models and model-based cost-effectiveness analyses as no conclusive data exist, even from the two largest prostate cancer screening trials.[4, 5] Such models simulate the progression of prostate cancer in the absence and presence of organised screening programmes, requiring data on the sensitivity of such programmes in order to simulate the number of cases detected and managed in each PSA testing round relative to a pool of undetected histological cancers. These models need to simulate the clinical incidence of prostate cancer during and after screening, this requires data on both the sensitivity of screening and clinical detection rates relative to histological cancer.

This is challenging as the gold standard procedure required to identify histological cancer involves the removal and step section biopsies (full slicing of the prostate gland into thin sections) undertaken during a full autopsy of the gland. Application of this 'gold standard' is not possible in screening studies, leading to verification bias, as only those with a PSA level above a chosen cut-point are referred for biopsy (and not all diagnosed with cancer will receive surgery). Those below the PSA cut-off or for whom cancer was

not detected at biopsy do not undergo any step-section biopsy of the prostate gland. Furthermore, needle biopsies cannot be viewed as an alternative gold standard procedure as their sensitivity can be as low as 30% relative to histological cancer. [7, 8] New approaches to prostate cancer diagnosis include the use of high quality Magnetic Resonance Imaging (MRI), which may increase rates of detection, particularly for anteriorly situated cancers. [9]

In this study, we estimate the proportion of histological cancers that were detected after a single round of population-based PSA testing (i.e. sensitivity) among UK men, stratified by PSA cut-off level; the true prevalence of histological prostate cancer in the UK and the clinical detection rate in the absence of organised screening.

2. Methods

2.1. Data and framework

Prostate ‘screening programme’ refers to the entire patient pathway from the initial PSA test to biopsy and diagnostic tests for those with a PSA level above a specified cut-point (e.g. 3 or 4ng/ml). The outcome is prostate cancer detection or no cancer detection.

Box 1. Apparent and true prevalence of disease

- Apparent prevalence: number of men testing positive by a diagnostic test (conditional on the initial PSA being above a specified cut-off level) divided by the total number of men screened in the population;
- True prevalence: actual number of men with histological prostate cancer divided by the number of men in the population.

Expanding previous methodology,[10] we used the association between true prevalence (TP) (see Box 1), based on a definitive gold standard procedure for the screen population (i.e. step-section at autopsy amongst men who died of causes other than prostate cancer), and apparent prevalence (AP) of prostate cancer, based on diagnostic testing of individuals with raised PSA levels in the screened population (i.e. prostate biopsy (initial and repeats), digital rectal examination, free-to-total PSA, magnetic resonance imaging (MRI) or computerised tomography (CT) scans),[11]

$$AP = TP \times sens + (1 - TP) \times (1 - spec) \quad \text{Equation (1)}$$

where *sens* and *spec* represent the sensitivity and specificity of the screening programme. Equation (1) can be arranged to inform the screening programme sensitivity relative to histological prostate cancer, i.e. proportion of all prostate cancers (TP) actually detected on screening, as,

$$sens = \frac{AP}{TP} \quad \text{Equation (2)}$$

where the specificity of the ‘screening programme’ is assumed to be 100% following diagnostic testing as it is very unlikely that men will be wrongly confirmed as having prostate cancer following all diagnostic tests post initial PSA and biopsy testing. Hence, this conceptualisation of specificity is different from the specificity of the initial prostate biopsy test which is high but not perfect.[7] Furthermore, by focusing on screen attenders, we explicitly excluded the screening attendance rate so that it can be added subsequently as an independent input.

Likewise, cancer detection data in non-screen populations represents the apparent prevalence (AP) in Equation (2) but the *sens* component now refers to the proportion of histological cancers detected clinically in areas without formal screening, i.e. sensitivity of clinical detection or clinical detection rate.

Bibliographic databases were systematically searched for studies reporting on the sensitivity of PSA screening and biopsy testing relative to histological cancer (see online appendix).[7, 8, 12] UK cancer registries and national databases were interrogated for data on the clinical incidence of cancer. Data on a single round of population-based PSA testing among UK men came from the ongoing UK-based Prostate testing for cancer and Treatment trial (ProtecT) (personal communication from ProtecT). Table 1 reports the identified evidence.

2.2. True prevalence of prostate cancer

We used 25 autopsy studies from a systematic review [6] to estimate the association between histological cancer and age as a continuous variable (odds ratio (OR) of 1.06 per year increase in age in predominantly white populations) using a Bayesian logistic meta-regression (see online appendix). This provided informed prior distributions of the parameters of true prevalence of histological cancer in age i , $P_{0,i}$.

2.3. UK-specific data on screening prevalence

We obtained screening prevalence data by age-group and PSA cut-off level (3 and 4ng/ml) from the diagnostic phase of the ongoing UK-based ProtecT trial examining treatment options for screen detected men (Table 1, $i=1,...,8$).[13] In this trial, men aged 50 to 69 years old in general practices in and around nine cities in the UK were invited to

attend an appointment for a PSA test between 2001 and 2009. Those with a PSA level above the 3ng/ml cut-off were recommended to receive a standardised protocol of digital rectal examination and transrectal ultrasound-guided needle biopsy. Men diagnosed with clinically localised prostate cancer were invited to participate in the trial of treatments.[13]

Using Equation (2), the sensitivity of the single round of the ‘screening programme’, $\theta_{i,j}$, was estimated by dividing the screening prevalence at age i and PSA cutoff level j (3 and 4ng/ml), $prev_{i,j}^{SCR}$, by the respective histological prevalence of prostate cancer, $P_{0,i}$,

$$\theta_{i,j} = \frac{prev_{i,j}^{SCR}}{P_{0,i}} \quad \text{for } i=1,...,4 \text{ } j=1,2$$

The sensitivity of the ‘screening programme’ was further assumed to be a function of the proportion of histological cancers at age i with PSA levels above the screening cut-off level j ($psa_{i,j}^{PCa}$); biopsy acceptance rate at age i ($bupt_i$) and the sensitivity of the biopsy procedure to detect histological cancer ($bsens^{PSA}$),

$$\theta_{i,j} = psa_{i,j}^{PCa} \times bupt_i \times bsens^{PSA} \quad \text{for } i=1,...,4 \text{ } j=1,2$$

The biopsy acceptance rate, $bupt_i$, was informed by the diagnostic phase of the ProtecT trial (Table 1, $i=20,...,24$). An autopsy study [12] provided data on the sensitivity of 12-core needle biopsy, $bsens^{PSA}$, relative to histological cancers with PSA values equal or above 4ng/ml (Table 1, $i=17$). The authors reported the sensitivity of needle biopsy to be similar for histological cancers with PSA values below and above 4ng/ml (53% and 59%, respectively) and we assumed the sensitivity of needle biopsy for cancers above PSA 3 and 4ng/ml to be the same.

The proportion of histological cancers with PSA levels above the 3ng/ml and 4 ng/ml cutoff ($psa_{i,j}^{PCa}$) was estimated using data from the ProtecT trial and from the autopsy study. [12] The proportion of men screened with PSA levels above cut-off level j ($psa_{i,j}^{ALL}$) is a weighted average of the proportion of men with and without histological cancer ($psa_{i,j}^{PCa}$ and $psa_{i,j}^{NoPCa}$, respectively) that have PSA levels above cutoff level j . The weights used correspond to the true prevalence of histological cancer, $P_{0,i}$,

$$psa_{i,j}^{ALL} = psa_{i,j}^{PCa} P_{0,i} + psa_{i,j}^{NoPCa} (1 - P_{0,i}) \quad \text{for } i=1,...,4 \text{ } j=1,2$$

Iguchi et al. 2008 [12] reported the proportion of histological cancers with PSA above 4ng/ml to be 47% in an autopsy series of men deceased with no known history of prostate cancer (Table 1, $i=19$). The expected proportion of histological cancers with PSA 3-3.9ng/ml was informed by adjusting data from control arm of the Prostate Cancer Prevention Trial (PCPT) using the ProtecT screening round (see online appendix) [14] The adjustment was needed because men in the PCPT were not representative of the patients in ProtecT as they underwent annual PSA screening during the 7 years of the trial before the final biopsy. The adjusted proportion of cancers with PSA above 3ng/ml was 53% compared to 32% reported in the PCPT study.[14]

2.4. UK-specific data on clinical incidence

Cancer registry data on the number of incident prostate cancer cases by 5-year age groups were obtained for England and Wales for 1995, 2005 and 2012 from the UK Office of National Statistics (ONS) (Table 1, $i=24,...,59$). The year 2005 was chosen to match the median year when patients were diagnosed in the screened prevalence data from ProtecT.

Using Equation (2), the clinical detection rate in areas lacking an organised population-based screening programme (sensitivity of clinical diagnosis), $\phi_{i,j}$, at age i and year j ($j=1995, 2005, 2012$), was estimated by dividing the proportion of incident cases in the population, $prev_{i,j}^{CLI}$, by the respective histological prevalence of prostate cancer, $P_{0,i}$,

$$\phi_{i,j} = \frac{prev_{i,j}^{CLI}}{P_{0,i}} \quad \text{for } i=1, \dots, 11$$

The incidence rates were estimated using the entire male population alive in each 5-year age group i and in year j (i.e. 1995, 2005 and 2012) and were assumed to be constant within each age group. These were then converted into proportions, $prev_{i,j}^{CLI}$ (see online appendix).

2.5. Statistical methods

A Bayesian framework was used to synthesise all available data using likelihood functions (e.g. binomial and Poisson processes) to link the observed data (e.g. prevalence of PSA detected prostate cancer from the single round of population-based PSA testing in ProtecT) with the unknown parameters (e.g. sensitivity of screening programme), update any prior information available, and simultaneously estimate joint posterior distributions of the parameters of interest. The online appendix provides details on the different types of data and parameters being estimated, as well as a directed acyclic graph of the statistical framework. Modelling was carried out using Bayesian Markov Monte Carlo (MCMC) methods in WINBUGS v.1.4.3.[15] Model selection was based on the posterior corrected mean deviance (Dbar) and the Deviance Information Criterion (DIC).[16, 17]

3. Results

Table 2 reports the evidence synthesis framework results. The histological prevalence of cancer by age was estimated to increase from 3% (95%CI: 2%-3%) at age 30 to 66% (95%CI: 61%-71%) by age 100. The sensitivity of the screening programme and of clinical diagnosis (in its absence), relative to histological cancer, also increased with age with the latter decreasing in men aged 80 years and over across the 3 time periods studied (see Appendix Table A.3). The sensitivity of the screening programme with a PSA cut-off of 3ng/ml varied between 15% (95%CI: 12%-17%) at age 50-54 and 34% (95%CI: 30%-37%) at age 65-69 (See Appendix Figure A.5). As expected, adopting a lower PSA level for referring patients for needle biopsy resulted in higher sensitivity relative to histological cancer. For example, adopting a PSA cut-off level of 3ng/ml, the sensitivity of the single round of the 'screening programme' at age 55-59 was estimated at 22% (95%CI: 19%-25%) compared to 15% (95%CI: 13%-18%) if adopting a 4ng/ml cut-off. In contrast, the clinical detection rate in the absence of mass screening, relative to histological cancer, varied between 0.2%-0.7% at age 50-54 and 1.2%-2.7% at age 65-69 from 1995 to 2012 (see Appendix Figure A.4). The overall model fit was good ($D_{res}=58.2$ compared to 55 data points).

The model estimates were fairly robust to changes in the prior distributions. However, the assumption and prior distribution for the precision (variance) of the proportion of histological cancers above and below the PSA cut-off had an impact on both the model fit and estimates (see online appendix). For example, assuming that the distribution of PSA levels in histological cancers is constant across age (i.e. fixed), the model fit was poor ($D_{res}=285.3$, compared to 55 data points).

4. Discussion

This paper presents a framework to estimate the histological prevalence of prostate cancer and the proportion of prostate cancers detected by a single round of a screening programme, i.e. sensitivity, when it is not possible to observe this directly. This was achieved by simultaneously synthesising data from the diagnostic phase of the UK ProtecT trial of treatment for localised prostate cancer, data on the incidence of clinically detected disease and prior information on the histological prevalence of prostate cancer in the population.

We estimated the sensitivity of the screening programme to vary between 15% (95%CI: 12%-17%) at age 50-54 and 34% (95%CI: 30%-37%) at age 65-69, using a PSA cut-off level of 3ng/ml, and 10% (95%CI: 8%-11%) at age 50-54 and 24% (95%CI: 21%-28%) at age 65-69 using a PSA cut-off level of 4ng/ml. This is in contrast with clinical detection rates relative to histological cancer of 0.7% (95%CI 0.6%-0.8%) to 2.7% (95%CI: 2.4-3.0) for these age groups in 2012. Other studies have reported estimates of sensitivity, but none is directly comparable to ours. The PCPT trial reported estimates of the sensitivity of screening in a US population to be 32.2% and 20.5% at PSA cut-off levels of 3ng/ml and 4ng/ml. This was estimated by performing 6-core biopsies in all patients at the end of the 7 year trial and estimating the proportion of detected cases with a PSA value above each cut-off level out of all biopsy detected cases [14]. However, other researchers have shown 6-core biopsies to have a sensitivity of 30% relative to histological cancer.[7] Hence, the PCPT trial estimates refer to prostate cancer detectable with a 6-core biopsy which represents a small proportion of the histological cancer population. Gann et al. [18] estimated the sensitivity to be 72% at a cut-off of 4ng/ml, by estimating how many clinical cases had their PSA values raised within a year before

detection. However, their estimates refer to clinically diagnosed cases (not histological cancers) and assume that these would have been present at the time of the PSA test.

Our proposed framework and results will enable the explicit incorporation of model inputs, such as the sensitivity of screening programmes and prevalence of cancer into prostate cancer modelling studies and cost-effectiveness analyses.[19, 20]. These important parameter inputs have either been excluded in previous cost-effectiveness analysis due to the lack of data[21, 22] or, if included, were informed by assumptions about its value, e.g. PSA sensitivity for local prostate cancer varying from 40% to 80%.[23] Finally, the use of UK-specific clinical incidence and screening prevalence enable the estimation of model parameters specific to this jurisdiction while also fully characterising all uncertainties, hence, avoiding ad hoc ‘tweaking’ of parameters to match external data.[21, 22]

There are several limitations to the approach used in this paper. First, our results are subject to the assumptions made about how the different data sources are associated with each other. For example, we assumed the cancers detected in the US-based autopsy study [12] to be similar to the pool of histological cancers in the screened UK population. We judged these populations to be similar as the autopsy population consisted of men, predominantly white, with no known history of prostate cancer where the prostate glands were examined using the step-section technique [7] and the detected cancers showed a similar distribution by age to UK based autopsies and our previous estimates [6]. Moreover, despite being a key parameter, data on PSA values in histological cancers are limited, consisting of the single autopsy study with 57 cancers without information on their age distribution. Understanding the PSA levels in histological cancers by age is as

important as determining the sensitivity of needle biopsy as the former will directly affect the screening detection rates (only those with a PSA level above a chosen cut-point are referred for biopsy). Hence, we tested several models and assumptions in sensitivity analysis concerning the autopsy data and the age of men with histological cancer. Also, we did not consider data from the PCPT trial on the distribution of PSA values in the biopsy detected cancers to be a valid proxy for histological cancers. As all men in the PCPT trial had annual measurement of PSA levels (PSA 4ng/ml cut-point) and digital rectal examination, we expect the proportion of cases below the cut-off level to be overrepresented. Furthermore, it would have been useful to have data on the sensitivity of needle biopsy relative to histological cancer for other PSA cut-off levels than 4ng/ml and avoid the assumption that it was the same for PSA cut-off levels of 3 and 4ng/ml.[12] Nonetheless, it may not be a strong assumption as there seems to be a weak correlation between detection rate and PSA levels as the sensitivity of needle biopsy was reported to be similar for histological cancers with PSA values below and above 4ng/ml. [12] Finally, whilst this analysis was undertaken using conventional PSA-testing as a cancer detection tool to trigger prostate biopsies, it is important to emphasise that if screening for prostate cancer were to be adopted in the future, methods will evolve to take into account other emerging biomarkers, genetic risk factors and imaging technologies in order to reduce unnecessary biopsies and over-diagnosis.[24] Nonetheless, the framework presented here can be easily expanded to explore the impact of these emerging screening technologies.

In conclusion, this study presents a framework for indirectly estimating important input parameters for diseases and cost-effectiveness models, such as sensitivity of a screening programme, for which no direct evidence exists. This was undertaken using a Bayesian

statistical framework to simultaneously combine all evidence sources and estimate means and distributions for the parameters of interest. The proposed method provides a transparent and systematic approach to make the best use of the available evidence and could be adapted to inform other jurisdictions and types of cancer. This will be of benefit to researchers and policy makers evaluating the impact of screening in their populations.

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Tables

Table 1. Sources of evidence used.

Ith	Data, region, year	(y/n)	Number of cases (y)	Sample size (n)	Ref
1	Screened detected cancer PSA \geq 3ng/ml, age 50-54	1.4%	288	20,761	ProtecT
2	Screened detected cancer PSA \geq 3ng/ml, age 55-59	2.8%	659	23,943	ProtecT
3	Screened detected cancer PSA \geq 3ng/ml, age 60-64	5.0%	978	19,558	ProtecT
4	Screened detected cancer PSA \geq 3ng/ml, age 65-69	7.1%	1,065	14,899	ProtecT
5	Screened detected cancer PSA \geq 4ng/ml, age 50-54	0.9%	178	20,761	ProtecT
6	Screened detected cancer PSA \geq 4ng/ml, age 55-59	1.8%	435	23,943	ProtecT
7	Screened detected cancer PSA \geq 4ng/ml, age 60-64	3.5%	687	19,558	ProtecT
8	Screened detected cancer PSA \geq 4ng/ml, age 65-69	5.2%	779	14,899	ProtecT
9	Men with PSA \geq 3ng/ml, age 50-54	4.3%	886	20,761	ProtecT
10	Men with PSA \geq 3ng/ml, age 55-59	8.2%	1,955	23,943	ProtecT
11	Men with PSA \geq 3ng/ml, age 60-64	14.1%	2,763	19,558	ProtecT
12	Men with PSA \geq 3ng/ml, age 65-69	19.7%	2,936	14,899	ProtecT
13	Men with PSA \geq 4ng/ml, age 50-54	2.1%	437	20,761	ProtecT
14	Men with PSA \geq 4ng/ml, age 55-59	4.5%	1,085	23,943	ProtecT
15	Men with PSA \geq 4ng/ml, age 60-64	8.3%	1,620	19,558	ProtecT
16	Men with PSA \geq 4ng/ml, age 65-69	12.4%	1,842	14,899	ProtecT
17	Sensitivity of biopsy relative to histological cancer with PSA \geq 4ng/ml, 12 core (MPZ+LPZ)	59.3%	16	27	Iguchi 2008
18	Histological cancers with PSA \geq 3ng/ml	53.4%	30	57	Iguchi 2008
19	Histological cancers with PSA \geq 4ng/ml	47.4%	27	57	Iguchi 2008
20	Men with biopsy out of PSA \geq 3ng/ml, age 50-54	90.2%	799	886	ProtecT
21	Men with biopsy out of PSA \geq 3ng/ml, age 55-59	90.3%	1,765	1,955	ProtecT
22	Men with biopsy out of PSA \geq 3ng/ml, age 60-64	88.5%	2,444	2,763	ProtecT
23	Men with biopsy out of PSA \geq 3ng/ml, age 65-69	86.6%	2,544	2,936	ProtecT
24	Incidence of prostate cancer, age 30-34, 1995	0.00%	0	2,027,900	ONS
25	Incidence of prostate cancer, age 35-39, 1995	0.00%	1	1,781,900	ONS
26	Incidence of prostate cancer, age 40-44, 1995	0.00%	10	1,650,800	ONS
27	Incidence of prostate cancer, age 45-49, 1995	0.00%	60	1,808,500	ONS
28	Incidence of prostate cancer, age 50-54, 1995	0.01%	213	1,471,100	ONS
29	Incidence of prostate cancer, age 55-59, 1995	0.05%	698	1,324,300	ONS
30	Incidence of prostate cancer, age 60-64, 1995	0.13%	1,551	1,206,700	ONS
31	Incidence of prostate cancer, age 65-69, 1995	0.25%	2,805	1,107,100	ONS
32	Incidence of prostate cancer, age 70-74, 1995	0.42%	4,052	971,300	ONS
33	Incidence of prostate cancer, age 75-79, 1995	0.62%	3,840	623,000	ONS
34	Incidence of prostate cancer, age 80-84, 1995	0.85%	3,448	407,900	ONS
35	Incidence of prostate cancer, age 85+, 1995	1.09%	2,549	233,100	ONS
36	Incidence of prostate cancer, age 30-34, 2005	0.00%	0	1,855,700	ONS
37	Incidence of prostate cancer, age 35-39, 2005	0.00%	8	2,055,300	ONS
38	Incidence of prostate cancer, age 40-44, 2005	0.00%	35	2,017,500	ONS
39	Incidence of prostate cancer, age 45-49, 2005	0.01%	193	1,765,100	ONS
40	Incidence of prostate cancer, age 50-54, 2005	0.04%	700	1,601,200	ONS
41	Incidence of prostate cancer, age 55-59, 2005	0.15%	2,505	1,714,100	ONS
42	Incidence of prostate cancer, age 60-64, 2005	0.29%	3,937	1,350,500	ONS
43	Incidence of prostate cancer, age 65-69, 2005	0.50%	5,827	1,154,300	ONS
44	Incidence of prostate cancer, age 70-74, 2005	0.63%	6,024	958,500	ONS
45	Incidence of prostate cancer, age 75-79, 2005	0.73%	5,458	748,400	ONS
46	Incidence of prostate cancer, age 80-84, 2005	0.77%	3,889	507,300	ONS
47	Incidence of prostate cancer, age 85+, 2005	0.81%	2,556	317,000	ONS
48	Incidence of prostate cancer, age 30-34, 2012	0.00%	0	1,798,016	ONS
49	Incidence of prostate cancer, age 35-39, 2012	0.00%	9	1,707,213	ONS
50	Incidence of prostate cancer, age 40-44, 2012	0.00%	70	1,901,368	ONS
51	Incidence of prostate cancer, age 45-49, 2012	0.02%	330	1,939,398	ONS
52	Incidence of prostate cancer, age 50-54, 2012	0.06%	1,105	1,748,433	ONS
53	Incidence of prostate cancer, age 55-59, 2012	0.17%	2,618	1,509,855	ONS

54	Incidence of prostate cancer, age 60-64, 2012	0.34%	4,961	1,476,180	ONS
55	Incidence of prostate cancer, age 65-69, 2012	0.57%	7,779	1,358,608	ONS
56	Incidence of prostate cancer, age 70-74, 2012	0.69%	6,723	972,550	ONS
57	Incidence of prostate cancer, age 75-79, 2012	0.80%	6,249	777,026	ONS
58	Incidence of prostate cancer, age 80-84, 2012	0.74%	3,983	538,259	ONS
59	Incidence of prostate cancer, age 85+, 2012	0.81%	3,307	406,695	ONS

MPZ: Mid peripheral zone, LPZ: lateral peripheral zone.

Table 2. Estimated parameters (mean and 95%CI)

Parameters	Mean	Low 95%CI	High 95%CI
Sensitivity of biopsy relative to histological cancer (%)	48	45	50
Sensitivity of screening round with $PSA \geq 3ng/ml$ at age 50-54 (%)	15	12	17
Sensitivity of screening round with $PSA \geq 3ng/ml$ at age 55-59 (%)	22	19	26
Sensitivity of screening round with $PSA \geq 3ng/ml$ at age 60-64 (%)	31	27	34
Sensitivity of screening round with $PSA \geq 3ng/ml$ at age 65-69 (%)	34	30	37
Sensitivity of screening round with $PSA \geq 4ng/ml$ at age 50-54 (%)	10	8	11
Sensitivity of screening round with $PSA \geq 4ng/ml$ at age 55-59 (%)	15	13	18
Sensitivity of screening round with $PSA \geq 4ng/ml$ at age 60-64 (%)	21	18	25
Sensitivity of screening round with $PSA \geq 4ng/ml$ at age 65-69 (%)	24	21	28
Clinical detection rate at age 50-54 (%), 1995	0.2	0.1	0.2
Clinical detection rate at age 55-59 (%), 1995	0.4	0.4	0.5
Clinical detection rate at age 60-64 (%), 1995	0.8	0.7	0.9
Clinical detection rate at age 65-69 (%), 1995	1.2	1.1	1.4
Clinical detection rate at age 50-54 (%), 2005	0.5	0.4	0.5
Clinical detection rate at age 55-59 (%), 2005	1.2	1.0	1.3
Clinical detection rate at age 60-64 (%), 2005	1.8	1.6	2.0
Clinical detection rate at age 65-69 (%), 2005	2.4	2.1	2.7
Clinical detection rate at age 50-54 (%), 2012	0.7	0.6	0.8
Clinical detection rate at age 55-59 (%), 2012	1.4	1.2	1.6
Clinical detection rate at age 60-64 (%), 2012	2.1	1.8	2.3
Clinical detection rate at age 65-69 (%), 2012	2.7	2.4	3.0
Histological cancer at age 30 (%)	3	2	3
Histological cancer at age 40 (%)	5	4	6
Histological cancer at age 50 (%)	8	7	10
Histological cancer at age 60 (%)	14	12	16
Histological cancer at age 70 (%)	23	21	26
Histological cancer at age 80 (%)	36	32	40
Histological cancer at age 90 (%)	51	46	56
Histological cancer at age 100 (%)	66	60	71
Proportion of histological cancers with $PSA \geq 3ng/ml$ (50-54) (%)	34	28	40
Proportion of histological cancer with $PSA \geq 3ng/ml$ (55-59) (%)	52	44	59
Proportion of histological cancer with $PSA \geq 3ng/ml$ (60-64) (%)	73	64	81
Proportion of histological cancer with $PSA \geq 3ng/ml$ (65-69) (%)	81	73	88
Proportion of men without cancer with $PSA \geq 3ng/ml$ (50-54) (%)	1.2	0.7	1.7
Proportion of men without cancer with $PSA \geq 3ng/ml$ (55-59) (%)	1.9	1.2	2.7
Proportion of men without cancer with $PSA \geq 3ng/ml$ (60-64) (%)	2.6	1.4	3.9
Proportion of men without cancer with $PSA \geq 3ng/ml$ (65-69) (%)	3.2	1.4	4.9
Proportion of histological cancers with $PSA \geq 4ng/ml$ (50-54) (%)	22	18	26
Proportion of histological cancer with $PSA \geq 4ng/ml$ (55-59) (%)	35	30	40
Proportion of histological cancer with $PSA \geq 4ng/ml$ (60-64) (%)	51	45	57
Proportion of histological cancer with $PSA \geq 4ng/ml$ (65-69) (%)	59	52	66
Proportion of men without cancer with $PSA \geq 4ng/ml$ (50-54) (%)	0.0	0.0	0.0
Proportion of men without cancer with $PSA \geq 4ng/ml$ (55-59) (%)	0.0	0.0	0.0
Proportion of men without cancer with $PSA \geq 4ng/ml$ (60-64) (%)	0.0	0.0	0.0
Proportion of men without cancer with $PSA \geq 4ng/ml$ (65-69) (%)	0.0	0.0	0.0
pD	51.5		
Dres	58.2		
DIC	109.7		

pD: effective number of parameters; DIC: deviance information criterion; Dres: sum of individual deviance residual contributions of data points.